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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,802	02/09/2004	Kari Alitalo	28967/34891.1	9059

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EXAMINER	
DANG, IAN D	

ART UNIT	PAPER NUMBER
1647	

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10/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,802	ALITALO, KARI	
	Examiner	Art Unit	
	IAN DANG	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46,48,50-53,61-64,67-70,72-75 and 77-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46,48,62,67,72-75 and 78-98* is/are allowed.

6)☒ Claim(s) *50-53,61,63,64,68-70 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02/09/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Upon further consideration, new issues are being raised. Therefore, finality has been withdrawn and prosecution on the merits continues. The final action was mailed 6/13/2008.

Status of Application, Amendments and/or Claims

The amendment of 08 August 2008 has been entered in full. Claims 1-45, 47, 49, 54-60, 65-66, 71, 76, have been cancelled and claims 46 and 67 have been amended.

Claims 46, 48, 50-53, 61-64, 67-70, 72-75, 77-98 are under examination.

Specification

The disclosure is objected to because of the following informalities:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction is required.

New Grounds of Rejection

Claim Rejections - 35 USC § 112, Second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 68-70 and 77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 68 and 77 are indefinite because they are dependent on the cancelled claim 66. Claims 69 and 70 are also rejected, since they depend on claim 68.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 50, 51, 52, 53, 61, 63, and 64 remain rejected under double patenting over claims 10, 11, 12, 17, 32, 33, and 34 and 53 of US Patent 6,824,777.

At page 16 of the response filed 08/08/2008, Applicants contend that the rejection of claims 43, 44, 49, 54-60, 71 and 76 is moot in view of the cancellation of these claims. In addition, Applicants indicate that claim 46 has been amended to incorporate the subject matter of claim 47, which the Examiner has already indicated as being allowable. Finally, Applicants indicate that the Examiner confirmed in a telephone call with the undersigned on July 23, 2008, that independent claims 50, 61 and 62 are also directed to allowable subject matter.

Although Applicant's response and amendments made to claim 46 have overcome the rejection of claim 46 under double patenting, claims 50, 51, 52, 53, 61, 63, and 64 remain rejected under double patenting over claims 10, 11, 12, 17, 32, 33, and 34 and 53 of US Patent 6,824,777. On July 23, 2008, the Examiner has mistakenly indicated that claims 50 and 61 are directed to an allowable subject matter.

Claim 50 is drawn to a method for antagonizing the function of Flt4 receptor tyrosine kinase (Flt4) in an organism, comprising administering to the organism a composition comprising a bispecific antibody, or fragment thereof, wherein said antibody or fragment specifically binds Flt4 and specifically binds a blood vascular endothelial marker antigen; and wherein said organism has a neoplastic disorder characterized by blood vessels comprising endothelial cells that express Flt4 corresponding to claim 10 of the US Patent 6,824,777. Claim 10 is drawn to a method for antagonizing the function of Flt4 receptor tyrosine kinase (Flt4) in an organism that expresses Flt4, comprising a step of administering to the organism a composition comprising a Flt4 antibody or Flt4 binding fragment thereof in a pharmaceutically acceptable carrier.

Although claim 10 does not disclose a bispecific antibody binding to blood vascular endothelial marker antigen, claim 50 of this instant application and claim 10 of the US Patent 6,824,777 are not patentably distinct because Flt 4 antibody encompasses the bispecific antibody of claim 50 and the Flt4 receptor tyrosine kinase (Flt4) expressed by vascular endothelials are known to express blood vascular endothelial cell marker antigen.

In addition, claim 51 of the instant application is drawn to an organism that is a human matching the limitations of claim 11 of the US Patent 6,824,777.

Finally, claim 52 of the instant application is drawn to a composition further comprising an anti-neoplastic agent conjugated to an antibody or antibody fragment matching the limitations of claim 12 of the US Patent 6,824,777.

Claim 53 is drawn to a method of inhibiting neoplastic cell growth in a mammalian subject, comprising: (a) screening a mammalian subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells that express Flt4; and (b) administering a composition to a mammalian subject identified according to step (a) as having a neoplastic disorder characterized by cells expressing Flt4, said composition comprising an inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, thereby inhibiting Flt4-mediated proliferation of said Flt4-expressing cells, wherein said inhibitor comprises a polypeptide selected from the group consisting of: (i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody; (ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody (iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and wherein said organism has a neoplastic disorder characterized by blood vessels comprising endothelial cells that express Flt4 matching the limitations of claim 17 of US 6,824,777.

Claim 17 is drawn to a method of inhibiting neoplastic cell growth in a mammalian subject, comprising steps of: (a) screening a mammalian subject to identify a neoplastic disorder characterized by cells expressing Flt4 receptor tyrosine kinase (Flt4); and (b) administering a composition to a mammalian subject identified according to step (a) as having a neoplastic disorder characterized by cells expressing Flt4, said composition comprising an inhibitor of the

binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, thereby inhibiting Flt4-mediated proliferation of said Flt4-expressing cells, wherein said inhibitor comprises a polypeptide selected from the group consisting of: (i) a polypeptide comprising an antigen binding fragment of an anti Flt4 antibody; and (ii) a polypeptide comprising a soluble Flt4 fragment, wherein said fragment and said polypeptide are capable of binding to an Flt4 ligand.

Although claim 17 does not recite the inhibitor comprising (ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody, the inhibitors of claim 17 encompass (ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody, claim 53 of this instant application and claim 17 of the US Patent 6,824,777 are not patentably distinct because the antibodies to VEGF-C and VEGF-D or polypeptide comprising an antigen binding fragment to antibodies to VEGF-C and VEGF-D are well known to inhibit proliferation of Flt4-expressing cells. Although claim 17 of the '777 does not include the inhibitor comprising (ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody, the anti-VEGF-C antibody and anti-VEGF-D antibody would be an inhibitor of neoplastic cell growth.

Claim 53 is drawn to a method of inhibiting neoplastic cell growth in a mammalian subject, comprising: (a) screening a mammalian subject to identify a neoplastic disorder characterized by blood vessels that comprise endothelial cells that express Flt4; and (b) administering a composition to a mammalian subject identified according to step (a) as having a neoplastic disorder characterized by cells expressing Flt4, said composition comprising an

inhibitor of the binding of an Flt4 ligand protein to Flt4 expressed in cells of said subject, thereby inhibiting Flt4-mediated proliferation of said Flt4-expressing cells, wherein said inhibitor comprises a polypeptide selected from the group consisting of: (i) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Flt4 antibody; (ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody (iv) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and wherein said organism has a neoplastic disorder characterized by blood vessels comprising endothelial cells that express Flt4 matching the limitations of claim 53 of US 6,824,777.

Claim 53 of US 6,824,777 is drawn to a method of treating a human having breast cancer characterized by endothelial cells that express Flt4 tyrosine kinase (Flt4), comprising a step of administering to said human a composition, said composition comprising an inhibitor of binding between Flt4 ligand protein and Flt4 expressed in cells of said human, thereby inhibiting Flt4 function, wherein the inhibitor comprises a polypeptide comprising an Flt4 binding fragment of human prepro-VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent.

Although claim 53 of the '777 does not include the inhibitor comprising (ii) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody;(iii) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody, the anti-VEGF-C antibody and anti-VEGF-D antibody would be an inhibitor of neoplastic cell growth.

Claim 61 is drawn to a method of treating a mammal having breast cancer characterized by blood vessel endothelial cells that express Flt4 tyrosine kinase (Flt4), comprising administering to said mammal a composition, said composition comprising an inhibitor of binding of an Flt4 ligand protein to Flt4 expressed in cells of said organism, thereby inhibiting Flt4 function, wherein the inhibitor comprises a member selected from the group consisting of:(a) an anti-Fit4 antibody or a polypeptide comprising an antigen binding fragment of said anti-Fit4 antibody; (b) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-C antibody; (c) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment of said anti-VEGF-D antibody; (d) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21); and (e) a polypeptide comprising an Flt4 binding fragment of human prepro- VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent matching the limitations of claim 32 of US 6,824,777.

Claim 32 is drawn to a method of treating a mammal having breast cancer characterized by endothelial cells that express Flt4 tyrosine kinase (Flt4), comprising a step of administering to said mammal a composition, said composition comprising an inhibitor of binding between Flt4 ligand protein and Flt4 expressed in cells of said organism, thereby inhibiting Flt4 function, wherein the inhibitor comprises a member selected from the group consisting of: (a) an anti-Flt4 antibody or a polypeptide comprising an antigen binding fragment thereof; (b) an anti-VEGF-C antibody or a polypeptide comprising an antigen binding fragment thereof; (c) an anti-VEGF-D antibody or a polypeptide comprising an antigen binding fragment thereof; and (d) a soluble polypeptide comprising a fragment of Flt4, wherein the polypeptide and the fragment are capable of binding to human VEGF-C (SEQ ID NO: 21).

Although claim 32 does not recite a polypeptide comprising an Flt4 binding fragment of human prepro- VEGF-C (SEQ ID NO: 21) or human prepro-VEGF-D (SEQ ID NO: 22) conjugated to an antineoplastic agent, claim 61 of this instant application and claim 32 of the US Patent 6,824,777 are not patentably distinct because claim 35 recites a polypeptide comprising an Flt4 binding fragment of human prepro- VEGF-C (SEQ ID NO: 21) and claim 36 recites the inhibitors further comprises an anti-neoplastic agent conjugated to the antibody or polypeptide in combination with claim 32 encompass the limitations of claim 61 of the instant application.

In addition, claim 63 of the instant application is drawn to a mammal that is a human matching the limitations of claim 33 of the US Patent 6,824,777.

Finally, claim 64 of the instant application is drawn to a screening step preceding the administering step matching the limitations of claim 34 of the US Patent 6,824,777.

Conclusion

Claims 50, 51, 52, 53, 61, 63, 64, 68-70, and 77 are not allowed. Claims 46, 48, 62, 67, 72-75, 78-98 are allowable.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IAN DANG whose telephone number is (571)272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
October 6, 2008

/Robert Landsman/
Primary Examiner, Art Unit 1647